REMARKS

With entry of this Amendment, claims 1-16, and 18-61 are pending in the application. Claims 1-8, 11-14, 18-35, 44, 45, and 50-61 are withdrawn from consideration. Claim 17 is canceled. Claims 9, 10, 15, 16, 36-43, and 46-49 are rejected.

The following rejections are pending:

- a. claims 9, 10, 15-17, 36-43, and 46-49 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification, Office Action mailed March 25, 2004 ("Office Action") at pages 4-10, and as allegedly lacking written description support in the specification, *id.* at pages 10-13;
- b. claims 9, 10, 15, 17, 36, 38, 40, 41, 46, and 47 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, *id.*, page 14;
- c. claims 15, 36, and 38 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Curtis et al., J. Biol. Chem. 263: 13779-13785 1988 ("Curtis"), id., page 15;
- d. claims 9,10, 15, 16, and 36-39 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,721,114 ("the '114 patent"), *id.*, pages 15-16;
- e. claims 15, 46, and 47 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Curtis in view of U.S. Patent No. 5,116,964 ("the '964 patent") and U.S. Patent No. 5,408,038 ("the '038 patent"), *id.*, page 17;

- f. claims 15, 16, and 46-49 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the '114 patent in view of the '964 patent, *id.*, pages 17-18;
- g. claims 15, 36, 37, 38, 40, and 41 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Curtis in view of U.S. Patent No. 5,824,784 ("the '784 patent") and the '038 patent, *id.*, pages 18-20; and
- h. claims 15, 16, and 38-43 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the '114 patent in view of the '784 patent, *id.*, pages 20-21.

Applicants thank the Examiner for extending the courtesy of an interview to their undersigned representative on May 17, 2004. Amendments to claims 9, 10, 15, and 16 that the Examiner indicated would obviate the enablement and written description rejections were discussed. In addition, the construction of the transitional phrase "consisting essentially of" in Applicants' claims was discussed. Distinctions between the pending claims and the Curtis reference were also discussed.

Applicants amend claims 9, 10, 15, and 16, as discussed with the Examiner. In particular, claims 9 and 10 are amended to delete subparts (i) and (k) through (o) without prejudice to or disclaimer of the subject matter recited therein. In addition, claims 9 and 10 are amended to encompass the sequences recited in subparts (a) to (h) encoding polypeptides having one or more conservative amino acid substitutions, which were encompassed by certain cancelled subparts. The Examiner acknowledged that claims encompassing one or more conservative amino acid substitutions were enabled. Support for this amendment may be found, for example, at pages 25 to 27 of

the specification as-filed. Amended claims 9 and 10 recite that polypeptides having one or more conservative amino acid substitutions inhibit tumor necrosis factor or interleukin 1 production by monocytes. Support for that amendment may be found throughout the Examples and Figures, for example, in Fig. 8 and at page 100. As requested by the Examiner, claims 9 and 10 are also amended to recite "A process for making an apo- A-I fragment T-cell activation inhibitor-like polypeptide fragment" rather than "An apo- A-I fragment T-cell activation inhibitor-like polypeptide fragment produced by a process." Support for that amendment may be found, for example, at pages 36 to 49 of the original specification.

In addition, claims 9 and 10 are amended to correct a clerical error in the numbering of fragments derived from SEQ ID NO:1. It would be obvious to one skilled in the art that the nucleotide numbers recited by subparts (a), (c), and (e) of claims 9 and 10 were incorrect and did not correspond with the intended encoding sequences. For example, claim 9(e) recited "a nucleotide sequence as set forth in residues 485 to 820 of SEQ ID NO: 1." One skilled in the art, however, would recognize that SEQ ID NO:1 ends at nucleotide 801. Subtracting 19 nucleotides from 485 and 820 produces a fragment from 466 to 801 of SEQ ID NO:1, which encodes the polypeptide recited in claim 9(h), i.e., residues 156 to 267 of SEQ ID NO:2. Similarly, one skilled in the art would have recognized that subparts (a) and (c) of claims 9 and 10 were intended to recite nucleotide sequences encoding the polypeptides recited, respectively, by subparts (b) and (d) of those claims. Corresponding corrections are made to the specification.

Claim 15 is amended to delete subparts (f) through (i) without prejudice to or disclaimer of the subject matter recited therein. In addition, claim 15 is amended to encompass the sequences recited in subparts (a) to (e) having one or more conservative amino acid substitutions, which were encompassed by certain cancelled subparts. Support for this amendment may be found, for example, at pages 25 to 27 of the original specification. Amended claim 15 recites that polypeptides that have one or more conservative amino acid substitutions inhibit tumor necrosis factor or interleukin 1 production by monocytes. Support for that amendment may be found throughout the Examples and Figures, for example, in Fig. 8 and at page 100.

Claim 16 is amended to delete subparts (a)(9) through (e) without prejudice to or disclaimer of the subject matter recited therein. In addition, claim 16 is amended to encompass the sequences recited in subpart (b)(1) to (b)(8) having one or more conservative amino acid substitutions, which were encompassed by certain cancelled subparts. Support for this amendment may be found, for example, at pages 25 to 27 of the original specification. Amended claim 16 recites that polypeptides that have one or more conservative amino acid substitutions inhibit tumor necrosis factor or interleukin 1 production by monocytes. Support for this amendment may be found throughout the Examples and Figures, for example, in Fig. 8 and at page 100.

No new matter is added by these amendments.

The Claims Are Enabled

The Examiner rejects claims 9, 10, 15-17, 36-43, and 46-49 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Office Action at page 4. The Examiner asserts, *inter alia*, that the transitional phrase "consisting

essentially of" in claims 9, 10, 15, and 16 is open ended and therefore expands the scope of the claims to encompass any polypeptide containing the recited sequences. See, e.g., Office Action at page 5.

Applicants respectfully traverse. The phrase "consisting essentially of limits the scope of a claim to the specified materials or steps 'and those that do not <u>materially</u> affect the <u>basic</u> and <u>novel</u> characteristic(s)' of the claimed invention." M.P.E.P. § 2111.03 (citing *In re Herz*, 537 F.2d 549, 551-52 (C.C.P.A. 1976)) (emphasis in original); see also Regents of the Univ. of California v. Eli Lilly and Co., 119 F.3d 1559, 1573 (Fed. Cir. 1997) (noting that the Examiner was correct in interpreting a claim reciting "human [proinsulin] **consisting essentially of** a plus strand having the sequence [nucleotides that encode human proinsulin]" to exclude fusion proteins (emphasis in original)).

Here, the specification makes it clear that the phrase "consisting essentially of" is not open-ended like the phrase "comprising." In fact, Applicants have identified between two embodiments: 1) "an isolated polypeptide consisting essentially of an amino acid sequence selected from . . ." (e.g., page 4, line 27, to page 5, line 13); and 2) "an isolated polypeptide comprising the amino acid sequence selected from . . ." (e.g., page 5, line 24, to page 6, line 15). Therefore, claims 9, 10, 15-17, 36-43, and 46-49 do not encompass an "indefinite number" of polypeptides and nucleic acids, as asserted by the Office. Office Action mailed October 22, 2002, at page 7. Instead, those claims literally encompass only sequences that do not "materially affect the basic and novel characteristic(s)" of the claimed AFTI polypeptide fragments.

M.P.E.P § 2111.03 advises that "[f]or the purpose of searching for and applying prior art under 35 U.S.C. § 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising.'" Here, however, the Examiner is construing "consisting essentially of" as 'comprising' in order reject the claims as allegedly being nonenabled, not for the purpose of applying prior art as suggested by the M.P.E.P. Moreover, the specification and claims do clearly identify the basic and novel characteristics of the invention: the polypeptide fragments of Apo AI that inhibit tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes.

Polypeptide fragments lacking that element are not literally encompassed by the claims.

The Examiner also rejects claims 9, 10, 15-17, 36-43, and 46-49 as allegedly not being enabled for the full scope of AFTI polypeptides that hybridize or share identity with, are allelic or splice variants of, or are otherwise related to the specific AFTI polypeptides disclosed in the specification. Office Action at page 8. As discussed during the May 17, 2004, interview and without acquiescing in the rejection, claims 9, 10, 15, and 16 are amended to delete certain subparts that recite AFTI polypeptides that hybridize or share identity with, are allelic or splice variants of, or are otherwise related to the specific AFTI polypeptides disclosed in the specification. The cancellation of claim 17 renders the rejection of that claim moot.

Applicants respectfully request the withdrawal of the rejection of claims 9, 10, 15, 16, and claims 36-43 and 46-49, which depend therefrom, under the enablement requirement of 35 U.S.C. § 112, first paragraph.

The Claims Are Supported by the Specification

The Examiner rejects claims 9, 10, 15-17, 36-43, and 46-49 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Office Action at page 10.

Applicants respectfully traverse. As discussed above with reference to the enablement rejection, the transitional phrase "consisting essentially of" in the claims is not appropriately construed as "comprising" for the purpose of making a written description rejection. Moreover, as also discussed above, the specification and claims, clearly identify the basic and novel characteristics of the invention.

The Examiner also asserts that the specification does not support the full scope of AFTI polypeptides that hybridize or share identity with, are allelic or splice variants of, or are otherwise related to the specific AFTI polypeptides encompassed by claims 9, 10, 15-17, 36-43, and 46-49. Office Action at pages 11-12. As discussed during the May 17, 2004, interview and without acquiescing in the rejection, claims 9, 10, 15, and 16 are amended to delete certain subparts that recite AFTI polypeptides that hybridize or share identity with, are allelic or splice variants of, or are otherwise related to the specific AFTI polypeptides disclosed in the specification. The cancellation of claim 17 renders the rejection of that claim moot.

Applicants respectfully request the withdrawal of the rejection of claims 9, 10, 15, 16, and claims 36-43 and 46-49, which depend therefrom, under the written description requirement of 35 U.S.C. § 112, first paragraph.

The Claims Are Definite

Claims 9, 10, 15, 17, 36, 38, 40, 41, 46, and 47 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office Action at page 14.

According to the Examiner, the recitation in these claims of the transitional phrase "consisting essentially of" followed by the recitation of "comprising" renders the claims "ambiguous, indefinite, and improper." *Id*.

Applicants respectfully traverse. Because the claims as amended recited only "consisting essentially of," however, this rejection is moot.

Applicants respectfully request the withdrawal of the rejection claims 9, 10, 15, 17, 36, 38, 40, 41, 46, and 47 as allegedly being indefinite.

The Claims Are Not Anticipated by Curtis

Claims 15, 36, and 38 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Curtis et al., J. Biol. Chem. 263: 13779-785, 1988 ("Curtis"). Office Action at page 15. According to the Examiner, Curtis discusses two fragments of Apo AI that are within the claims: EMSKDLEEVYAKVQPYLDDFQKKWQEEMELYRQKVE ("Curtis Sequence 1") and DEPPQSPWDRVKDLATVYVDVLK ("Curtis Sequence 2").

Applicants respectfully traverse. In order to anticipate a claim, a prior art reference must teach <u>every</u> limitation of the claim. See Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986) ("It is axiomatic

¹ Applicants note that neither of these sequences is actually a fragment of Apo AI. As indicated by the ellipses on both ends of the sequences, this is simply a partial representation of the entire Apo AI protein. The actual Apo AI fragments used by Curtis are depicted below the partial sequences identified by the Examiner and are much shorter.

that for prior art to anticipate under § 102 it has to meet every element of the claimed invention, and that such a determination is one of fact."). Here, the two sequences identified by the Examiner neither "comprise" nor "consist essentially of" the polypeptides recited by the claims. Curtis Sequence 1, for example, consists of amino acid residues 109 to 144 of SEQ ID NO: 2 and would be encoded by a nucleotide sequence consisting of nucleotides 325 to 432 of SEQ ID NO: 1. Likewise, Curtis Sequence 2 consists of amino acid residues 25 to 47 of SEQ ID NO: 2 and would be encoded by a nucleotide sequence consisting of nucleotides 73 to 142 of SEQ ID NO: 1.

In contrast, claim 15 recites a polypeptide fragment consisting essentially of an amino acid sequence selected from (a) an amino acid sequence as set forth in residues 25 to 194 of SEQ ID NO:2; (b) an amino acid sequence as set forth in residues 25 to 144 of SEQ ID NO:2; (c) an amino acid sequence as set forth in residues 156 to 267 of SEQ ID NO:2; (d) an amino acid sequence as set forth in residues 25 to 113 of SEQ ID NO:2; (e) an amino acid sequence as set forth in residues 25 to 113 of SEQ ID NO:2; (e) an amino acid sequence as set forth in residues 73 to 113 of SEQ ID NO:2, and (f) a polypeptide fragment as set forth in (a) to (e) having one or more conservative amino acid substitutions. Curtis' amino acid sequences are either significantly shorter than, or do not overlap at all with, the sequences recited in amended claim 15. For this reason, Curtis cannot anticipate claims 15 or claims 36 and 38, which depend therefrom, because those claims require that at least the recited sequence be present.

Applicants respectfully request the withdrawal of the rejection of claims 15, 36, and 38 under 35 U.S.C. § 102(b) over Curtis.

The Claims Are Not Anticipated by U.S. Patent No. 5,721,114

Claims 9, 10, 15, 16, and 36-39 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,721,114 to Abrahamsén et al. ("the '114 patent"). Office Action at page 15. According to the Examiner, the '114 patent discusses a 59 residue fragment consisting of amino acids 184-243 from the carboxyl terminus of Apo Al Milano. *Id.* As with Curtis, however, the fragment of the '114 patent neither "comprises" nor "consists essentially of" the sequences recited by the rejected claims. The fragment of the '114 patent consists of amino acid residues 209 to 267 of SEQ ID NO: 2 and would be encoded by nucleotides 625 to 801 of SEQ ID NO: 1.

The fragment of the '114 patent is shorter than the carboxyl terminal fragment recited by claims 9, 10, 15, and 16 and, therefore, cannot anticipate those claims or claims dependent thereon.

Applicants respectfully request the withdrawal of the rejection of claims 9, 10, 15, 16, and 36-39 under 35 U.S.C. § 102(b) over the '114 patent.

The Claims Are Not Obvious

The Examiner also rejects the claims under 35 U.S.C. § 103(a) as allegedly being unpatentable over various combinations of Curtis or the '114 patent with secondary documents, as follows:

claims 15, 46, and 47 are rejected over Curtis in view of U.S. Patent Nos. 5,116,964 and 5,408,038, Office Action at page 17;

claims 15, 16, and 46-49 are rejected over the '114 patent in view of U.S. Patent No. 5,116,964, *id.* at page 17-18;

claims 15, 36, 38, 40, and 41 are rejected over Curtis in view of U.S. Patent Nos. 5,824,784 and 5,408,038; *id.* at page 18-20; and

claims 15, 16, and 38-43 are rejected over the '114 patent in view of U.S. Patent No. 5,824,784, *id.* at page 20-21.

All of these rejections are based on the Examiner's position that Curtis and the '114 patent anticipate the AFTI polypeptide fragments encompassed by the claims. As Applicants have shown above, however, the amended claims are not anticipated by either reference. Moreover, neither Curtis nor the '114 patent suggests modifying the disclosed Apo A-I fragments to produce polypeptides consisting essentially of the sequences recited by the claims to produce fragments that inhibit tumor necrosis factor (TNF) or interleukin-1 (IL-1) production by monocytes.

The secondary documents fail to remedy the deficiencies of Curtis and the '114 patent. Therefore, Applicants assert that the Examiner has failed to establish that any of the combinations would have suggested apo-A-I polypeptide fragments according to any of the rejected claims. Moreover, Applicants need not address the Examiner's contentions concerning the various combinations with respect to other elements of certain claims. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

Applicants respectfully request the withdrawal of the rejections of claims 15, 16, 36, 38-43, and 46-49 under 35 U.S.C. § 103(a).

Other Matters

The Examiner indicates that if claim 9 is found allowable, claim 10 will be objected to as a substantial duplicate thereof. Office Action at page 2. Amended claims

9 and 10 recite different subject matter. In particular, claim 9 recites a process for making an apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment comprising culturing a *eukaryotic cell*. Claim 10 recites a process for making an apo-A-I fragment T-cell activation inhibitor-like polypeptide fragment comprising culturing a *prokaryotic cell*. Applicants submit that claim 10 is not a substantial duplicate of claim 9.

The Examiner objects to claims 9, 10, 15, and 16 because "apo-A-1" should read "apo-A-I." Office Action at page 2. Applicants have corrected the typographical error.

According to the Examiner, color photographs and color drawings were filed on August 17, 2002, without the petition required by 37 C.F.R. § 1.84(a)(2). Office Action at pages 2-3. Applicants records do not show that color photographs or drawings were filed in this matter. Applicants ask the Examiner to provide additional information regarding this issue so that they may comply with any applicable regulations.

The Examiner notes that sequence identifiers are missing from Figures 1C and 1D. Office Action at page 3. Amended versions of Figures 1C and 1D are submitted herewith, along with redlined copies of the original figures.

Finally, the Examiner objects to the specification because of informalities concerning the numbering of Figures 6 and 7. Office Action at page 3. Applicants have amended the specification to correct the informalities noted by the Examiner.

CONCLUSION

Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: September 24, 2004

William L. Strauss Reg. No. 47,114

Attachments: annotated drawing sheets

FULL LENGTH APO-A1 SEQUENCE

1
MKAAVLTLAVLFLTGSQARHFWQQDEPPQSPWDRVKDLATVYVD
VLKDSGRDYVSQFEGSALGKQLNLKLLDNWDSVTSTFSKLREQLGPVTQEFWDNLEKE
TEGLRQEMSKDLEEVKAKVQPYLDDFQKKWQEEMELYRQKVEPLRAELQEGARQKLHE
194
LQEKLSPLGEEMRDRARAHVDALRTHLAPYSDELRQRLAARLEALKENGGARLAEYHA
267
KATEHLSTLSEKAKPALEDLRQGLLPVLESFKVSFLSALEEYTKKLNTQ (SEQ TO NO. 2)

sig_peptide 20..91
mature_protein 92..820

20 a tgaaagctgc ggtgctgacc ttggccgtgc tcttcctgac

61 ggggagccag geteggeatt tetggeagea agatgaacce ceceagagee cetgggateg

121 agtgaaggae etggeeatt tgtaegtgga tgtgeteaaa gacageggea gagactatgt

181 gteecagttt gaaggeteeg cettgggaaa acagetaaac etaaagetee ttgaccaactg

241 ggacagegtg acetecacet teagcaaget gegegaacag eteggeeetg tgacccagga

301 gttetgggat aacetggaaa aggagacaga gggeetgagg caggagatga geaaggatet

361 ggaggaggtg aaggeeaagg tgcageeeta eetggacgae tteeagaaga agtggeagga

421 ggagatggag etetaeegee agaaggtgga geegetgege geagagetee aagagggege

481 gegeeagaag etgeaegage tgcaaggaa getgageeea etgggegagg agatgegega

541 eegegegee geeeatgtgg aegegetgeg eaegeatetg geeeeetaaca gegaegaget

601 gegeeagege ttggeegee geettgagge teteaaggag aaeggeggeg eeagaetgge

601 egagtaceae geeaaggeea eegageatet gageaegete agegagaagg eeaageege

721 getegaggae eteegeeaag geetgetgee egtgetggag agetteaagg teagetteet

781 gagegetete gaggagtaca etaagaaget eaacacceag (SEQ IO NO:1)

FIG. 1A

18K N-TERMINAL FRAGMENT

25
DEPPQSPWDRVKDLATVYVD

VLKDSGRDYVSQFEGSALGKQLNLKLLDNWDSVTSTFSKLREQLGPVTQEFWDNLEKE

TEGLRQEMSKDLEEVKAKVQPYLDDFQKKWQEEMELYRQKVEPLRAELQEGARQKLHE
LQEKLSPLGEEMRDRARAHVDALRTHLAPYSDEL (SEQ IONO:3)

92 gatgaaccc ccccagagcc cctgggatcg

121 agtgaaggac ctggccactg tgtacgtgga tgtgctcaaa gacagcggca gagactatgt

181 gtcccagttt gaaggctccg ccttgggaaa acagctaaac ctaaagctcc ttgaccactg

241 ggacagcgtg acctccacct tcagcaagct gcgcgaacag ctcggccctg tgacccagga

301 gttctgggat aacctggaaa aggagacaga gggcctgagg caggagatga gcaaggatct

361 ggaggaggtg aaggccaagg tgcagcccta cctggacgac ttccagaaga agtggcagga

421 ggagatggag ctctaccgcc agaaggtgga gccgctgcg gcagagctcc aagagggcgc

481 gcgccagaag ctgcacgagc tgcaagagaa gctgagccca ctgggcgagg agatgcgca

541 ccgcgcgcgc gcccatgtgg acgcgctgcg cacgcatctg gcccctaca gcgacgagct

601 g (SEQ IO NO:4)

13K N-TERMINAL FRAGMENT

25
DEPPQSPWDRVKDLATVYVD

VLKDSGRDYVSQFEGSALGKQLNLKLLDNWDSVTSTFSKLREQLGPVTQEFWDNLEKE

TEGLRQEMSKDLEEVKAKVQPYLDDFQKKWQEEMELYRQKVE (Portion of SEQ IONO) 3)

- 92 gatgaaccc ccccagagcc cctgggatcg
- 121 agtgaaggac ctggccactg tgtacgtgga tgtgctcaaa gacagcggca gagactatgt
- 181 gtcccagttt gaaggctccg ccttgggaaa acagctaaac ctaaagctcc ttgacaactg
- 241 ggacagcgtg acctccacct tcagcaagct gcgcgaacag ctcggccctg tgacccagga
- 301 gttctgggat aacctggaaa aggagacaga gggcctgagg caggagatga gcaaggatct
- 361 ggaggaggtg aaggccaagg tgcagcccta cctggacgac ttccagaaga agtggcagga
- 421 ggagatggag ctctaccgcc agaaggtgga g (Portion of SEP IONO: 4)

C 13K M-TERMINAL FRAGMENT

156 QKLHE

194
LQEKLSPLGEEMRD RARAHVDALRTHLAPYSDELRQRLAARLEALKENGGARLAEYHA

267
(Portion of SEQ ID NO: 2)

485 cagaag ctgcacgagc tgcaagagaa gctgagccca ctgggcgagg agatgcgca

541 ccgcgcgcg gcccatgtgg acgcgctgcg cacgcatctg gccccctaca gcgacgagct

601 gcgccagcgc ttggccgcgc gccttgaggc tctcaaggag aacggcggcg ccagactggc

661 cgagtaccac gccaaggcca ccgagcatct gagcacgctc agcgagaagg ccaagcccgc

721 gctcgaggac ctccgccaag gcctgctgcc cgtgctggag agcttcaagg tcagcttcct

781 gagcgctctc gaggagtaca ctaagaagct caacacccag (Portion of SEQ TO NO.)